

AMENDMENT TO THE SPECIFICATION

Please replace the paragraph on page 2, line 26, through page 3, line 5, of the specification with the following paragraph.

Both RAS and OLP have been treated with systemic and topical steroid therapy. Topical steroids for RAS and OLP have included fluocinonide (LIDEX® [Lidex]), Clobetasol propionate (TEMOVATE® [Temovate]), Halobetasol propionate (ULTRAVATE® [Ultravate]), Triamcinolone [Triamcinolone] acetonide (KENALOG® [Kenalog]), and Dexamethasone (DECADRON® [Decadron]). These agents have been used as ointments, gels, or rinses, and result in a reduction of symptoms because of their anti-inflammatory effect. There is no evidence to suggest that they ameliorate the severity of RAS ulceration or prevent its formation. It is questionable as to whether the duration of ulceration is affected. Topical steroids have provided the basis for the management of erosive lichen planus. More aggressive steroid or immunomodulatory therapy has been prescribed for bullous lesions. In general, topical steroids may control symptoms and reduce the severity of lesions.

Please replace the paragraph on page 3, lines 10-25, of the specification with the following paragraph.

I have discovered that combination therapy can be an effective treatment for RAS and OLP. The treatment involves administering to the patient two therapeutic agents: the first is an immunosuppressive agent, and the second is a compound that exerts activity

against TNF, either by blocking or antagonizing [antagonising] the TNF receptor, or, more preferably, interfering [interferring] with the production of TNF, e.g., by down-regulating transcription of the TNF gene. Both agents can be administered either topically or systemically; most preferably, both are administered topically to the lesion itself, in a carrier such as a rinse or gel. Preferred immunosuppressive agents are topical steroids or known immunosuppressive agents such as cyclosporin, FK 506, DECADRON® [Decadron], and triamcinolone [triamcimalone] acetonide. Anti-TNF agents include thalidomide and Pentoxifylline (PTX): 3,7-Dihydro-3,7-dimethyl-1-(5-oxohexyl)-1H-purine-2,6-dione, which is an analog of methylanthine theobromine. PTX, which was initially developed as an agent for the treatment of peripheral vascular disease, exerts cellular effects on platelets, endothelial cells, neutrophils, and macrophages; PTX also is known to have activity against TNF and interleukin [interlukin]-1. It appears to act by down-regulating transcription of the TNF gene.

Please replace the paragraph on page 4, lines 1-6, of the specification with the following paragraph.

Combination therapies of the invention include the following. [:]

- 1) A topical ointment or gel consisting of fluocinonide and PTX.
- 2) A topical rinse consisting of DECADRON® [Decadron] and PTX.
- 3) A topical rinse consisting of cyclosporin and PTX.

4) A topical gel or ointment consisting of triamcinolone [triamcinalone] acetonide and thalidomide.

5) A topical gel or rinse consisting of DECADRON® [Decadron] and thalidomide.

Please replace the paragraph on page 4, lines 19-25, of the specification with the following paragraph.

The patient was treated according to the invention as follows. The patient was given PTX tablets (one 400 mg tablet per day), combined with a rinse of the topical steroid DECADRON® [Decadron]. This treatment [treatment] completely resolved all of the patient's major lesions, after which time the patient was placed on a topical regimen pursuant to which he treats individual [individual] lesions with the DECADRON® [Decadron] rinse. The patient reported, approximately six months after initial treatment, that he was completely without mouth ulcers for the first time in eight years.